

Docket No. 1451.003US1
WD #431242



Affymetrix, Inc. Ref: 3248

CLAIMS

NUCLEIC ACID ANALYSIS USING COMPLETE N-MER ARRAYS

Applicant: Kevin L. Gunderson et al.

Serial No.: 09/394,230

- Sub 02
1. (Twice amended) A method of determining the presence of a mutation in a target polynucleotide, comprising the steps of:
 - (a) providing at least two identical polynucleotide probe microarrays, wherein each probe comprises a double stranded region and a single-stranded n-mer overhang region such that the overhangs in each array constitute a complete set of n-mers, wherein each n-mer is at least 8 nucleotides in length;
 - (b) hybridizing the target polynucleotide to said overhangs of probe polynucleotides in one microarray to generate a target hybridization pattern;
 - (c) hybridizing a reference polynucleotide to said overhangs of probe polynucleotides in a second microarray to generate a reference hybridization pattern; and
 - (d) determining the presence of a mutation in the target polynucleotide by comparing the reference and target hybridization patterns without sequencing the target polynucleotide.
 2. The method of claim 1, wherein in step b), the hybridized target polynucleotide is ligated to the probe.
 3. The method of claim 1, wherein in step c), the hybridized reference polynucleotide is ligated to the probe.
 4. The method of claim 1, wherein the overhangs have free 5'-ends.
 5. The method of claim 1, wherein the overhangs have free 3'-ends.

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6. The method of claim 1, wherein the n-mer comprises from about 4 to about 50 nucleotides.
7. The method of claim 1, wherein the mutation is a substitution mutation.
8. The method of claim 1, wherein the mutation is a deletion mutation.
9. The method of claim 1, wherein the mutation is an insertion mutation.
10. The method of claim 1, in which said target polynucleotide is selected from the group consisting of: a cystic fibrosis transmembrane conductance regulator gene, a p53 gene, a mitochondrial DNA, or an HIV gene.
11. (Amended) The method of claim 1, wherein the microarrays are arranged in parallel.
12. (Twice amended) A method of determining whether two or more target polynucleotides are identical without sequencing the target polynucleotides, comprising the steps of:
 - (a) providing at least two identical polynucleotide probe microarrays, wherein each probe comprises a double stranded region and a single-stranded n-mer overhang region such that the overhangs in each microarray constitute a complete set of n-mers, wherein each n-mer is at least 8 nucleotides in length;
 - (b) hybridizing first target polynucleotide to said overhangs of probe polynucleotides in one microarray to generate a first hybridization pattern;
 - (c) hybridizing second target polynucleotide to said overhangs of probe polynucleotides in a second microarray to generate a second hybridization pattern; and
 - (d) comparing the first and second hybridization patterns.

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13. The method of claim 12, wherein in step b), the hybridized target polynucleotide is ligated to the probe.
14. The method of claim 12, wherein in step c), the hybridized reference polynucleotide is ligated to the probe.
15. The method of claim 12, wherein the overhangs have free 5'-ends.
16. The method of claim 12, wherein the overhangs have free 3'-ends.
17. The method of claim 12, wherein the n-mer comprises from about 4 to about 50 nucleotides.

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18. (Amended) The method of claim 12, wherein the microarrays are arranged in parallel.
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